PROPOSED RESEARCH PROJECT
TO BE SUPPORTED
BY THE GESCHICKTER FUND FOR MEDICAL RESEARCH, INC.
AT [redacted]
(Effective July 1, 1960)

Project Title: The Synthesis and Biochemical Evaluation of Potential Psychopharmacological Agents.

Principal Investigator: [redacted], Professor and Head of the Department of Pharmaceutical and Medicinal Chemistry, College of Pharmacy.*

For the past several years, the applicant has been engaged in research involving (I) the synthesis of organic entities having potential effects upon the central nervous system, and (II) the evaluation of connections between the chemical and pharmacodynamic properties of these compounds. The applicant is primarily interested in the fundamental study of relationships between molecular constitution and biochemical response, and is particularly concerned with the effect of gradual changes in the chemical structure of synthetic entities upon isolated enzyme systems. The reader is referred to (A) reports submitted earlier to the Geschickter Fund for Medical Research, Inc. [1-7], and (B) published accounts [8-19] for supplemental information.

The applicant plans to continue his investigation in accordance with the principles set forth in the cited communications. Specifically, he intends to:

1. Synthesize several series of new compounds patterned after (a) organic amines known to affect the central nervous system, and (b) moieties acknowledged as substrates in enzyme systems implicated in the pharmacodynamics of compounds possessing psychopharmacological properties. The member compounds of each series will be designed with gradual changes in their constitution, or physical properties, or both; furthermore, they will be planned in such a manner that potential differences in the interaction between the member compounds of a given synthetic series and a given enzyme may be interpreted in terms of concepts reasonably well established in contemporary theoretical chemistry.

(b)(3)

2. Study the effect of these entities upon (a) isolated enzyme preparations believed to be associated with brain function, and (b) other plausible biochemical systems.

3. Explore relationships between the biochemical activity of each series of derivatives, and the successive changes in the chemical and physical characteristics of the member compounds.

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At present, our synthetic work is centered around series of arylalkylaminoalkylacetamides, and pyridine- and piperidinecarboxamides which could be visualized as moieties derived from the psychotomimetic molecule LSD (see Figures I, II, III and IV; other series have been planned).

Concurrently, the completed compounds are being evaluated in isolated cholinesterase systems in which LSD has shown remarkable specificity. Our manometric procedures

* Effective July 1, 1960 (on leave of absence July 1, 1960 through June 30, 1961).

yield very precise measurements of activity in isolated pseudo- and acetylcholinesterase systems, and enable us to evaluate the significance of even minor variations in activity due to small constitutional changes in a series of molecules.

We are aware of the fact that the effectiveness of a psychopharmacological agent in vitro cannot be interpreted as evidence for the involvement of the specific enzyme in the mechanism of psychotomimetic responses. Yet even without conclusive causal connection, this approach may furnish valuable information on the nature of psychopharmacological agents.

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It is felt that this investigation may yield (a) information assisting the elucidation of interrelationships between molecular constitution and biological response, (b) better insight into the biochemical characteristics and therapeutic potentialities of certain types of moieties, (c) several series of new organic compounds and information about their physical characteristics, and (d) data supplementing our knowledge of the neurochemical processes associated with the action of psychopharmacological agents.

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The references cited in the first paragraph of the outline are listed on the following page.

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January 22, 1960

[redacted]

cc: [redacted]

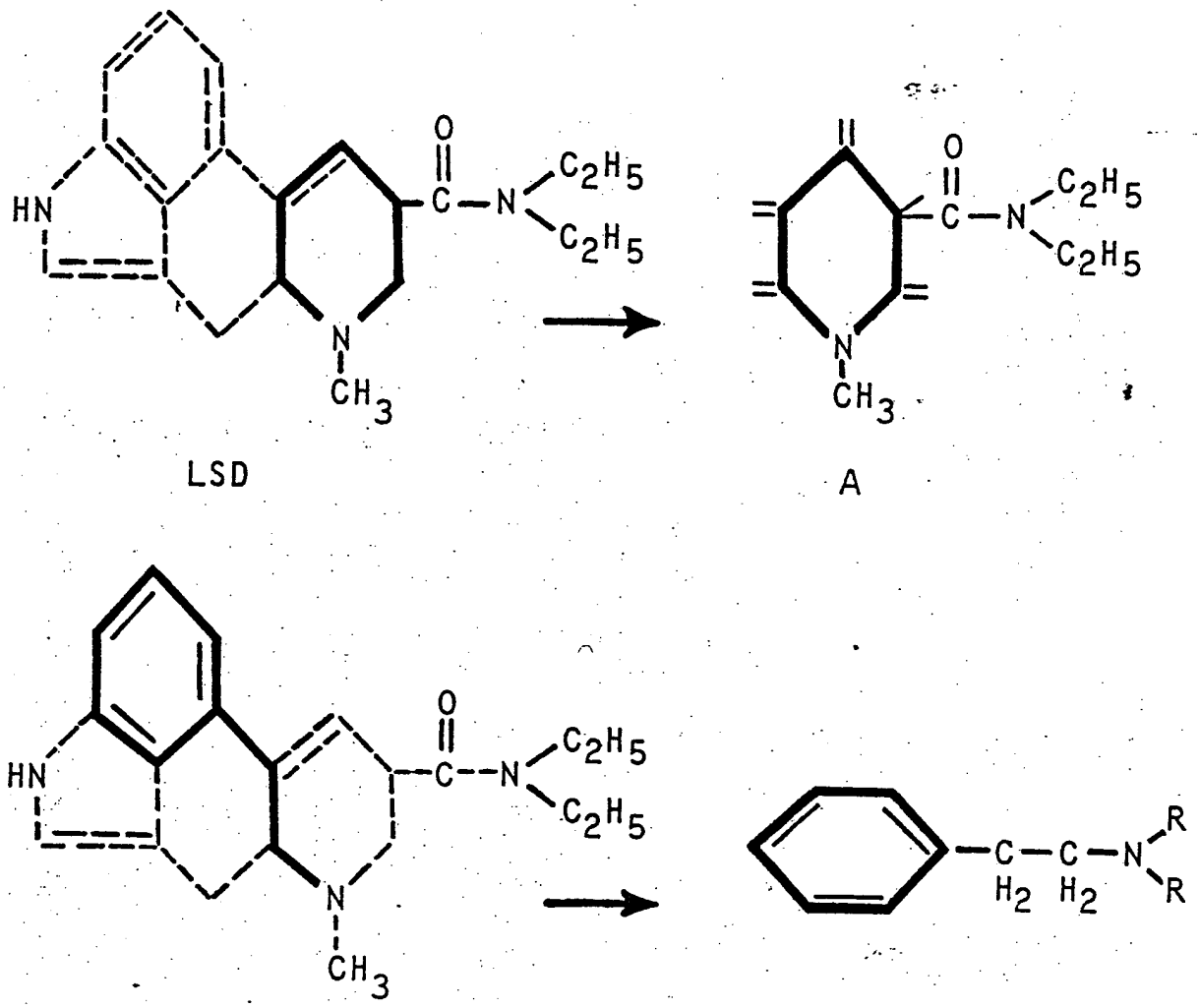

FIGURE 1.

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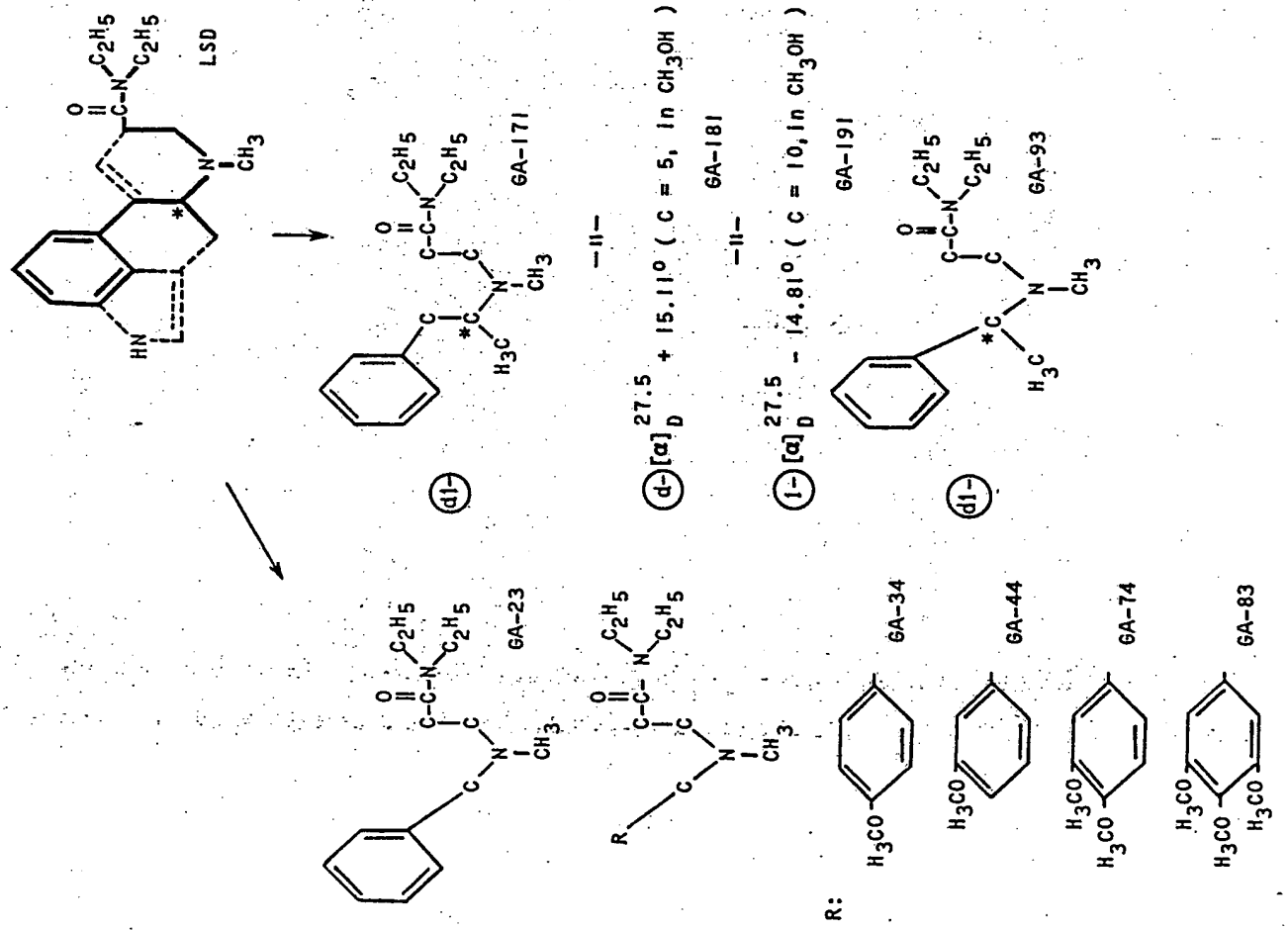

FIGURE II.

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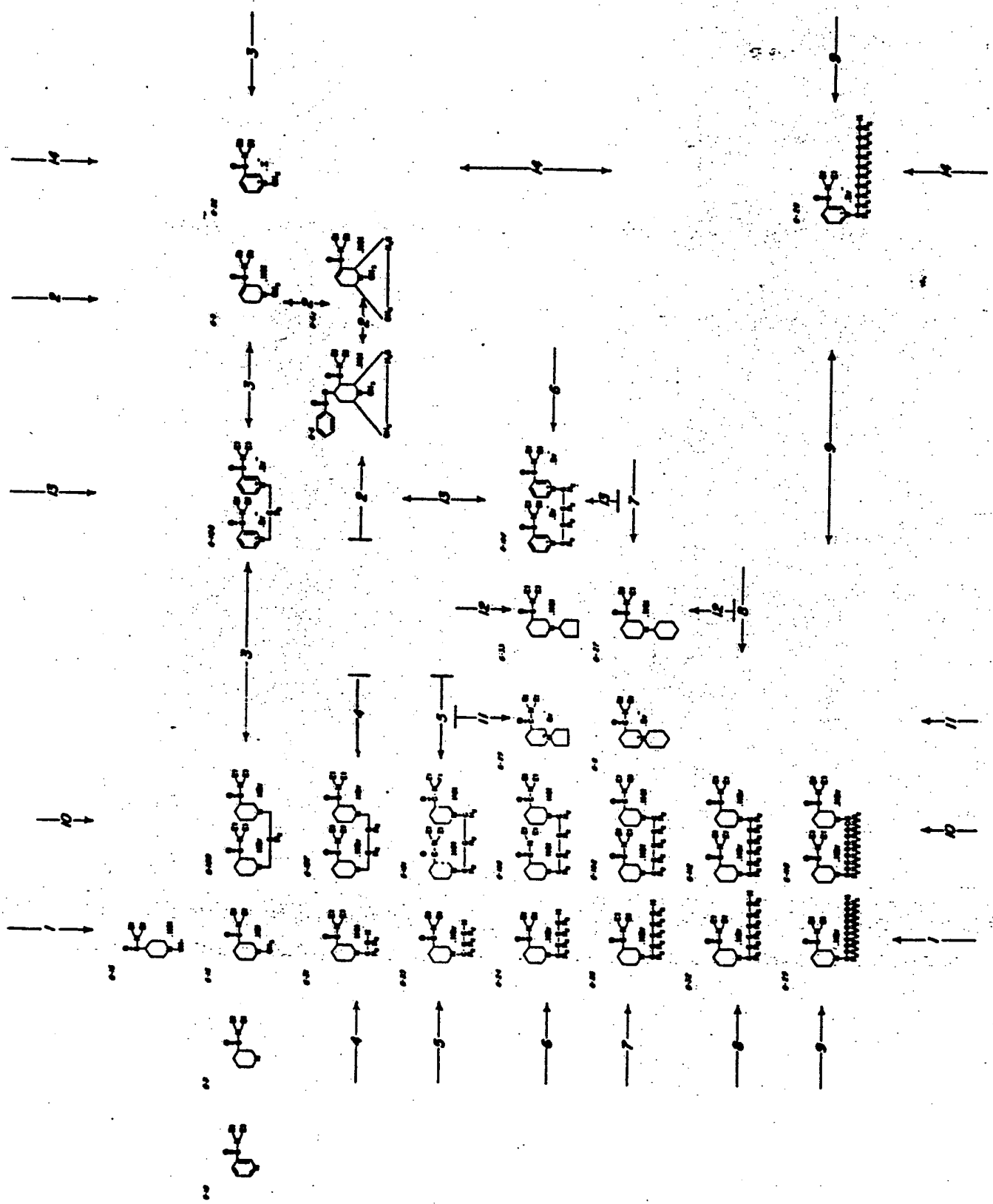
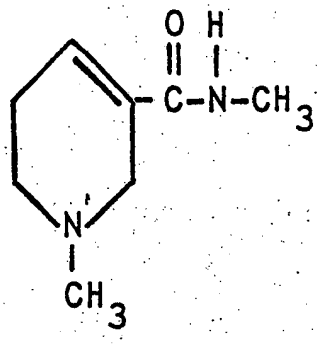
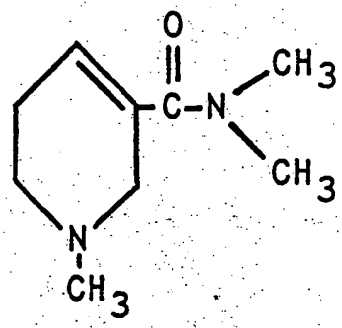
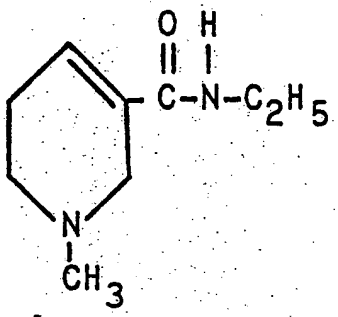


FIGURE III.







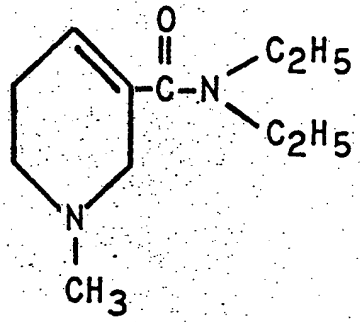


FIGURE IV.

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[redacted]